OBSERVATIONS

Association Between Oral Isotretinoin Therapy and Unmasked Latent Immuno-Mediated Diabetes

Isotretinoin is an effective drug for the treatment of acne, but elevated liver enzymes, dyslipidemia, insulin resistance, and type 2 diabetes during isotretinoin therapy have been reported. We recently managed a 28-year-old male outpatient (BMI 24 kg/m^2) affected by severe facial acne. There was no familial history of diabetes. All laboratory determinations, including hepatic function and fasting plasma glucose (FPG) levels (95 mg/dl), were in the reference range. C-peptide and A1C were not evaluated.

In July 2008, a dermatologist prescribed isotretinoin (30 mg/day) for the patient. After 1 month, the patient had an FPG of 118 mg/dl and a substantially normal lipid profile (total cholesterol [TC] 191 mg/dl, HDL cholesterol 34 mg/dl, LDL cholesterol 141 mg/dl, triglyceride [TG] levels 82 mg/dl, and normal hepatic parameters). Isotretinoin therapy was confirmed. Two months later, the patient's FPG was 147 mg/dl, TC 172 mg/dl, HDL cholesterol 29 mg/dl, LDL cholesterol 120 mg/dl, TG levels 118 mg/dl, with normal liver enzymes. In October 2008, FPG was 191 mg/dl, and in November 2008, the therapy was finally discontinued after the acne healed. FPG was 134 mg/dl, A1C 6.2% (<4.2%), and C-peptide level 1.09 ng/ml (0.9–3.9). We prescribed a low–glycemic index diet with no hypoglycemic drugs.

One month after isotretinoin withdrawal, the patient showed FPG 121 mg/dl, TC 159 mg/dl, HDL cholesterol 49 mg/dl, LDL cholesterol 98 mg/dl, TG 57 mg/dl, normal hepatic parameters, and a slight weight loss (−2 kg; BMI 23.4 kg/m^2). In January 2009, C-peptide was reduced to 1.0 ng/ml; the patient was negative for anti-islet cell antibodies though positive (5.7 IU/ml) for GAD antibodies. After 3 months of well-being, during which the patient failed to perform the recommended visits and blood exams, he complained of polydipsia, polyuria, and weight loss (−4 kg) with FPG 217 mg/dl, A1C 9.1% (<6.4%), TC 169 mg/dl, HDL cholesterol 50 mg/dl, LDL cholesterol 106 mg/dl, TG 63 mg/dl, C-peptide 0.8 ng/ml, and GAD antibodies 6.8 IU/ml, without ketosis. Regarding the poor glycemic control and low C-peptide levels, we prescribed intensive insulin therapy with lispro at mealtime and glargine at bedtime. After 3 months the patient regained weight (6.7 kg, BMI 24.2 kg/m^2), with a better metabolic control (FPG 121 mg/dl, A1C 6.4%, TC 182 mg/dl, HDL cholesterol 48 mg/dl, LDL cholesterol 121 mg/dl, TG 66 mg/dl, and C-peptide 0.6 ng/ml).

An insulin resistance worsening induced by isotretinoin therapy, probably related to higher lipid oxidation through the Randle cycle, is observed by Koistinen et al. (1). In fact, isotretinoin induced a reversible decrease in insulin sensitivity, evaluated by euglycemic clamp and the pathognomonic insulin resistance dyslipidemia. An association between metabolic syndrome and isotretinoin was previously reported (2). The lipotoxicity, glucotoxicity, and apoptosis of β-cells mediated by high levels of circulating fatty acids (3,4) are well known.

It is reasonable that latent autoimmune diabetes in adults (LADA) could be clinically revealed by drug-induced insulin resistance. In this case, the only remarkable change of lipid profile consisted in a reduction of HDL cholesterol during isotretinoin treatment; therefore, the previously reported physiopathological hypothesis (1–4) is not completely supported. However, this is the first report of an association between isotretinoin and an unmasking case of autoimmune diabetes.

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